

Advanced Regression: Linear and generalised linear models I

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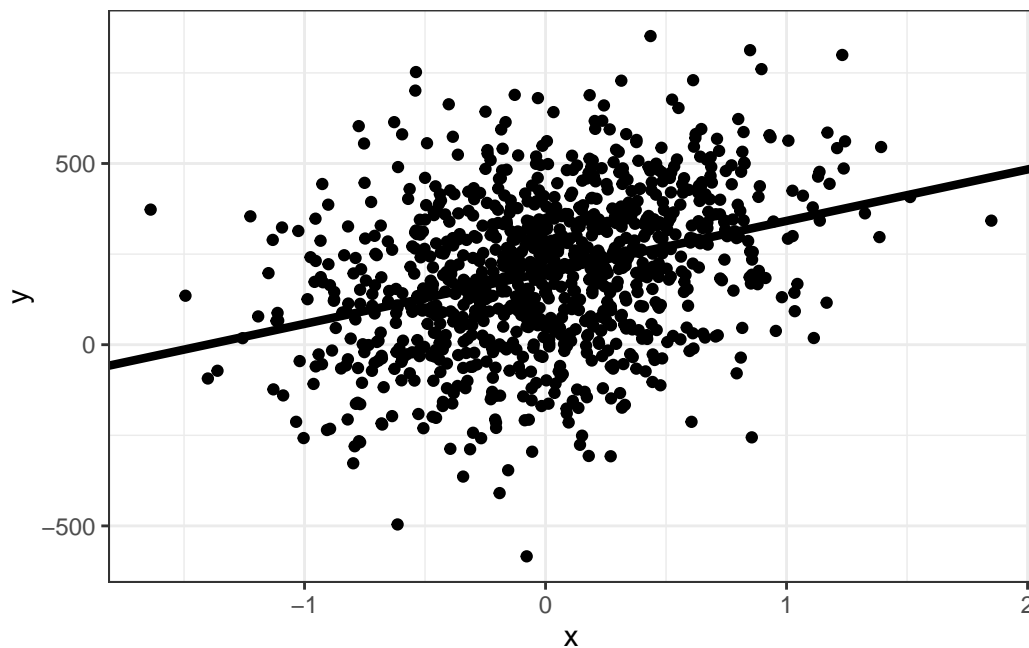
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Main goal of (linear) regression

Regression models are used to investigate association between

- an outcome variable y
- potential explanatory variables (or predictors) $x = (x_1, x_2, \dots, x_p)$

The statistical idea is to see if the $x = (x_1, x_2, \dots, x_p)$ can give an adequate description of the variability of the outcome y .



Motivations

1. **Understand** how the predictors affect the outcome.
 - Example: We conduct an observational study focusing on type 2 diabetes as outcome. Our aim is to understand which risk factors are associated with the risk of type 2 diabetes.
2. **Predict** the outcome of new observations, where only the predictors are observed, but not the outcome.
 - Example: We study type 2 diabetes and want to predict disease progression. Our aim is to identify individuals with poor prognosis and improve their treatment.

The linear model

$$y = \alpha + x\beta + \epsilon$$

- y : Outcome, response, dependent variable. Dimension: $n \times 1$
- x : Regressors, exposures, covariates, input, explanatory, or independent variables. Dimension: $n \times p$
- ϵ : Residuals, error. Dimension: $n \times 1$
- α : Intercept. Dimension: 1×1
- β : Regression coefficients. Dimension: $p \times 1$

Parameters to estimate:

- α : Intercept, Baseline level, the expected mean value of y when all $x = 0$
- $\beta = (\beta_1, \dots, \beta_p)$: vector of regression coefficients.
- β_j : : regression coefficients of variable x_j . The expected change in y for a one-unit change in x_j when the other covariates are held constant.

Observed data:

- y : Outcome or response.
- x : Regressors, exposures, covariates, input, explanatory or independent variables
 - $i = 1, \dots, n$ samples.
 - $j = 1, \dots, p$ variables.

Estimates: Ordinary least squares (OLS)

$$\hat{\beta}_{OLS} = \underbrace{(x^t x)^{(-1)}}_{p \times p} \underbrace{x^t}_{p \times n} \underbrace{y}_{n \times 1}$$

- Inversion of $\underbrace{(x^t x)^{(-1)}}_{p \times p}$ requires $x^t x$ to be of full rank (Lecture 2b).

Alternative representation:

- $\hat{\beta} = \frac{cov(x,y)}{cov(x)}$, where the sample covariance is defined as:
 - $cov(x,y) = \frac{1}{n} \sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})$
 - $cov(x) = \frac{1}{n} \sum_{i=1}^n (x_i - \bar{x})(x_i - \bar{x})$

Example: Diabetes data

- y : quantitative measure of disease progression one year after baseline (vector)
- x : predictor matrix
 - clinical parameters: age, sex, bmi
 - map: blood pressure
 - tc: total cholesterol
 - ldl: low-density lipoprotein
 - hdl: high-density lipoprotein
 - tch: total cholesterol over hdl
 - ltg: triglycerides
 - glu: glucose
- $n = 442$: sample size

The `lm()` command in R

```
lm(y ~ age + sex + glu + map + ltg, data = x)
```

Formula:

```
y ~ x1 + x2 + x3
```

- left of `~`: outcome
- right of `~`: predictors

It is also possible to enter a full matrix `x`, transform by `as.matrix()`, as multivariable set of predictors:

```
y ~ x
```

An intercept is always included, to turn off add `-1`

Interpreting the `summary.lm()` command

```
library(lars)
```

Loaded lars 1.3

```
library(dplyr)

data(diabetes)
x <- as.data.frame.matrix(diabetes$x)
y <- diabetes$y

lm(y ~ age + sex + glu + map + ltg, data = x) %>% summary.lm()
```

Call:

```
lm(formula = y ~ age + sex + glu + map + ltg, data = x)
```

Residuals:

Min	1Q	Median	3Q	Max
-----	----	--------	----	-----

-165.128 -43.025 -5.232 42.446 182.050

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	152.133	2.871	52.990	< 2e-16 ***
age	-54.227	65.854	-0.823	0.41071
sex	-166.066	62.903	-2.640	0.00859 **
glu	175.377	71.671	2.447	0.01480 *
map	426.532	70.342	6.064	2.89e-09 ***
ltg	706.395	70.929	9.959	< 2e-16 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 60.36 on 436 degrees of freedom

Multiple R-squared: 0.3939, Adjusted R-squared: 0.387

F-statistic: 56.68 on 5 and 436 DF, p-value: < 2.2e-16

Difference between univariable and multivariable regression

```
lm(y ~ glu, data = x) %>% summary.lm()
```

Call:

```
lm(formula = y ~ glu, data = x)
```

Residuals:

Min	1Q	Median	3Q	Max
-153.069	-57.716	-5.466	54.656	186.839

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	152.133	3.392	44.851	<2e-16 ***
glu	619.223	71.312	8.683	<2e-16 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 71.31 on 440 degrees of freedom

Multiple R-squared: 0.1463, Adjusted R-squared: 0.1444

F-statistic: 75.4 on 1 and 440 DF, p-value: < 2.2e-16

Reduction of the regression coefficient from 619 to 175 after conditioning on other covariates → attenuation of the effect

Further estimates

- Weighted least squares

$$\hat{\beta}_{WLS} = \underbrace{(x^t w x)}_{p \times p} \underbrace{x^t}_{p \times n} \underbrace{w}_{n \times n} \underbrace{y}_{n \times 1}$$

where w is a $n \times n$ diagonal weight matrix

- Maximum likelihood
- Bayesian linear regression (Module: Bayesian Statistics)

Fitted values and residuals

- Fitted values

$$\hat{y} = x\hat{\beta} = x \underbrace{(x^t x)^{-1} x^t}_h y$$

- Hat matrix h
- Residuals are the difference between the fitted values (predicted by the model) and the actual observed outcome: $r_i = \hat{y}_i - y_i$
- The residuals are a vector $r = (r_1, \dots, r_n)$ of length n .



Tip

Residuals are an important quantity for model diagnostics.

Fitted values and residuals

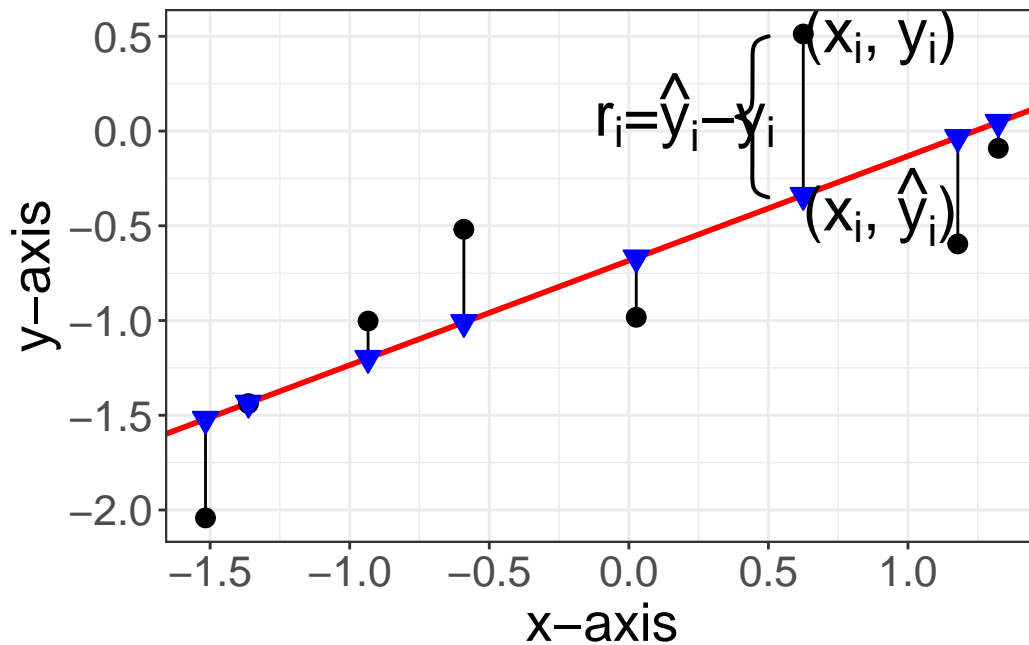
Warning: package 'ggrepel' was built under R version 4.3.1

Warning: package 'pBrackets' was built under R version 4.3.1

Warning in is.na(x): is.na() applied to non-(list or vector) of type 'expression'

Warning in is.na(x): is.na() applied to non-(list or vector) of type 'expression'

Warning in is.na(x): is.na() applied to non-(list or vector) of type 'expression'



lm(): Fitted values and residuals

- First fit a linear model and save it in the object lm0

```
lm0 <- lm(y ~ glu, data = x)
```

- The linear model object lm0 contains
 - Regression coefficients

```
lm0$coefficients
```

```
(Intercept)      glu
      152.1335    619.2228
```

– Fitted values

```
lm0$fitted.values
```

– Residuals

```
lm0$residuals
```

Assumptions

1. Linearity: There is a linear relationship between x and y .
2. Weak exogeneity: The predictors x are viewed as fixed variables; there is no measurement error on x .
3. Constant variance (homoscedasticity): All residuals have the same variance.
4. No perfect multicollinearity: No predictor can be expressed as a linear combination of the other predictors (Lecture 2b).
5. Independent errors: The residuals are uncorrelated (e.g. in time-series the error of time point t will depend on the error of time point $t - 1$) and independent of x .

Further assumptions

- Normal-distributed errors:

The residuals are normal-distributed.

Note: This is not required for the OLS estimate, but for the Maximum Likelihood estimation.

- Outlier: observation point that is distant from other observations.

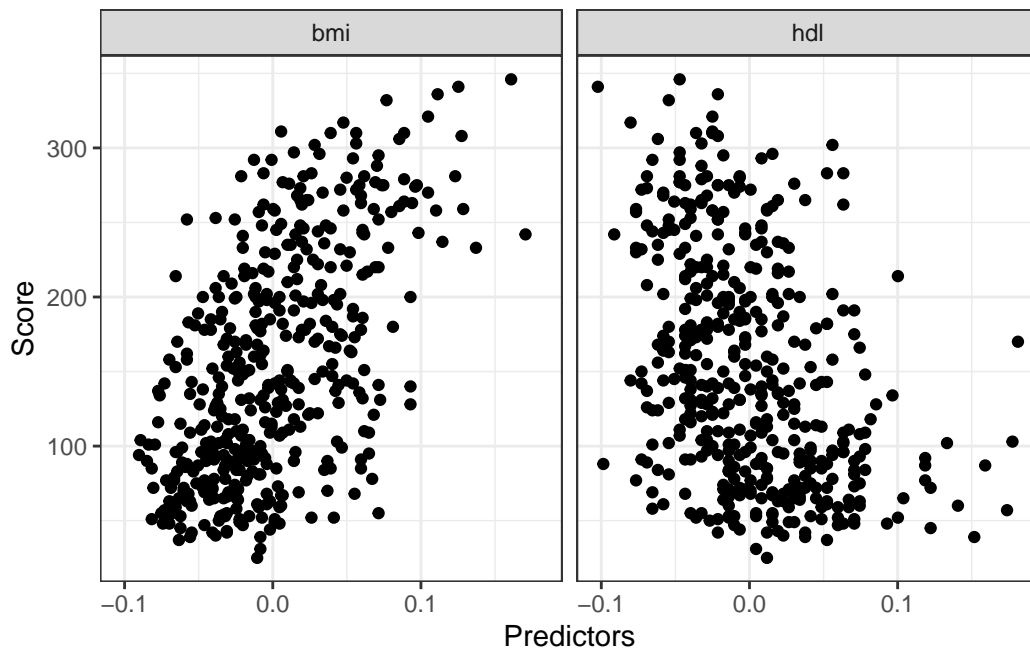
It is recommended to check the data for outliers, which can arise because of many reasons:

- Measurement error (remove)
- Errors in the pre-processing steps (fix or remove)
- “True” biological outliers (follow-up)

- Influential variants: Cook’s distance

Diagnostic plots: Linear relationship

- Scatterplot of y against x



Diagnostic plots: Linear relationship

- Scatterplot of residuals (y-axis) against fitted values (x-axis)

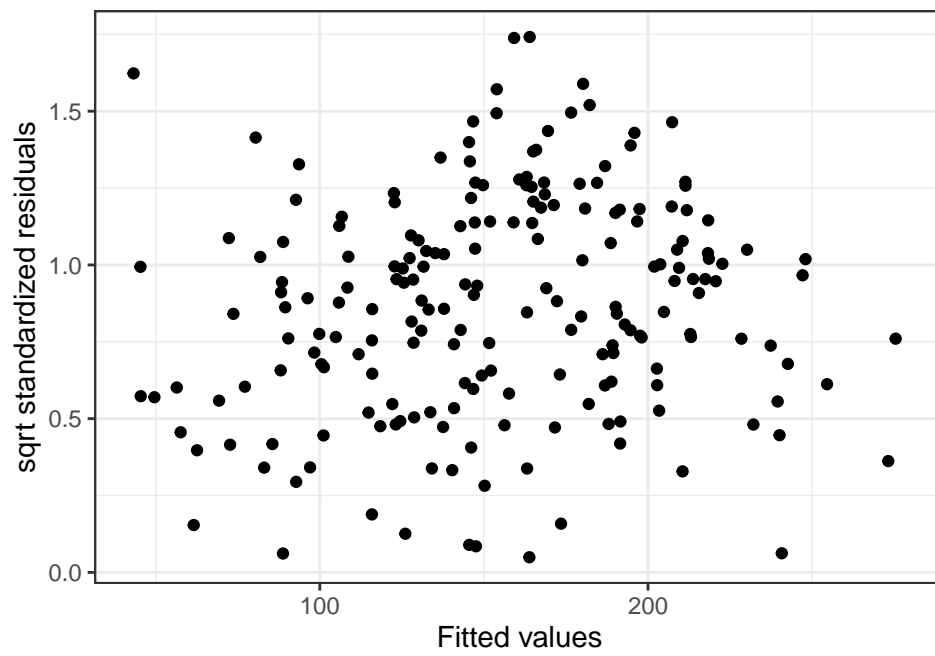
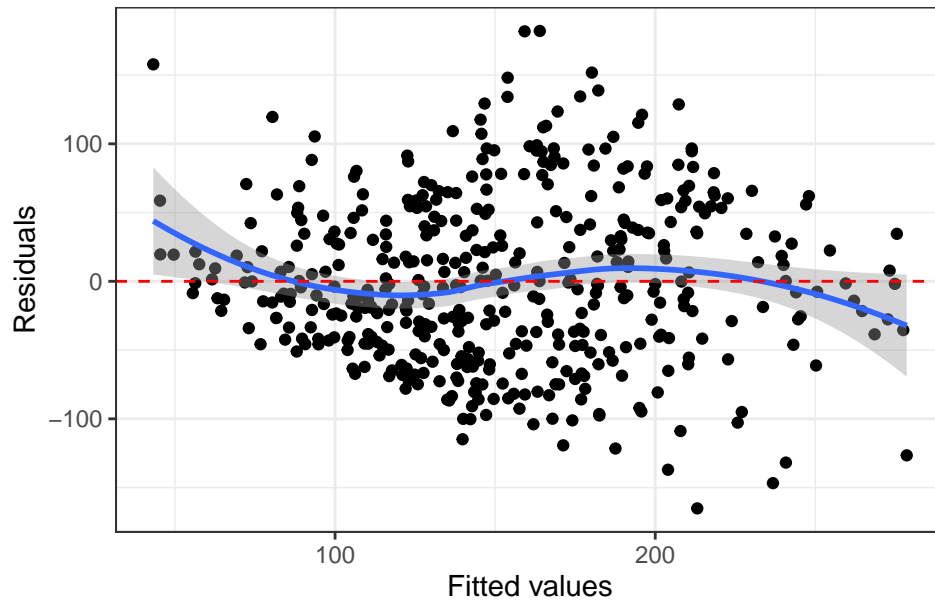
Diagnostic plots: Homoscedasticity

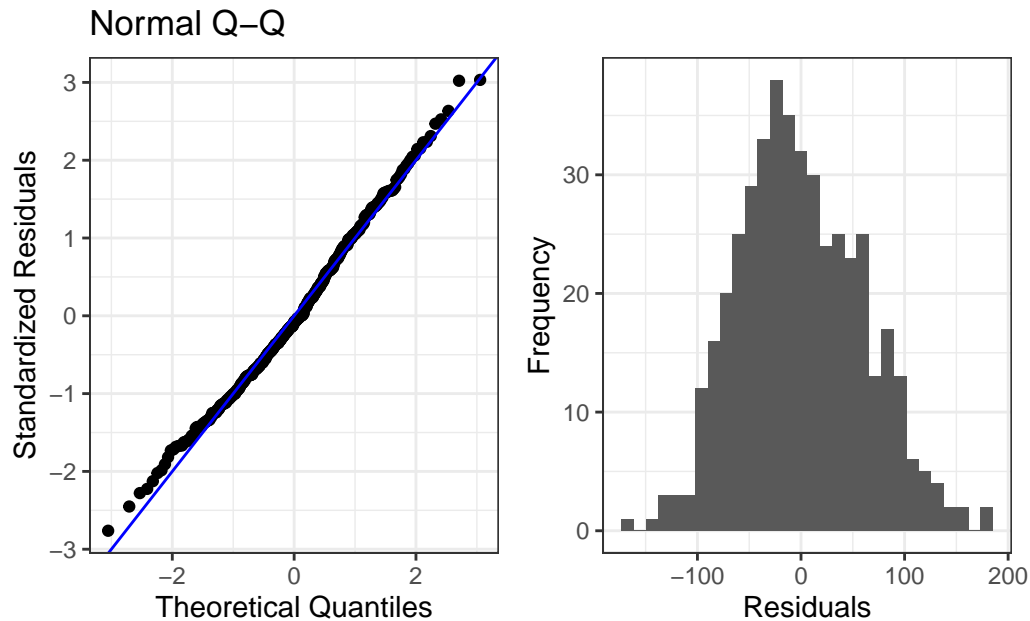
- Scatterplot of standardised residuals (y-axis) against fitted values (x-axis)

Diagnostic plots: Normal-distribution of residuals

- Q-Q plots of observed residuals (y-axis) against theoretical values under the Normal distribution (x-axis)

Residual vs Fitted Plot





Diagnostic plots: Outliers

- Scatterplot of standardised residuals against Cook's distance.
- Cook's distance measures the effect of deleting a given observation (sum of all the changes in the regression model when observation i is removed).

lm(): Diagnostics

- Linear relationship and outliers (Scatterplot of y against x)

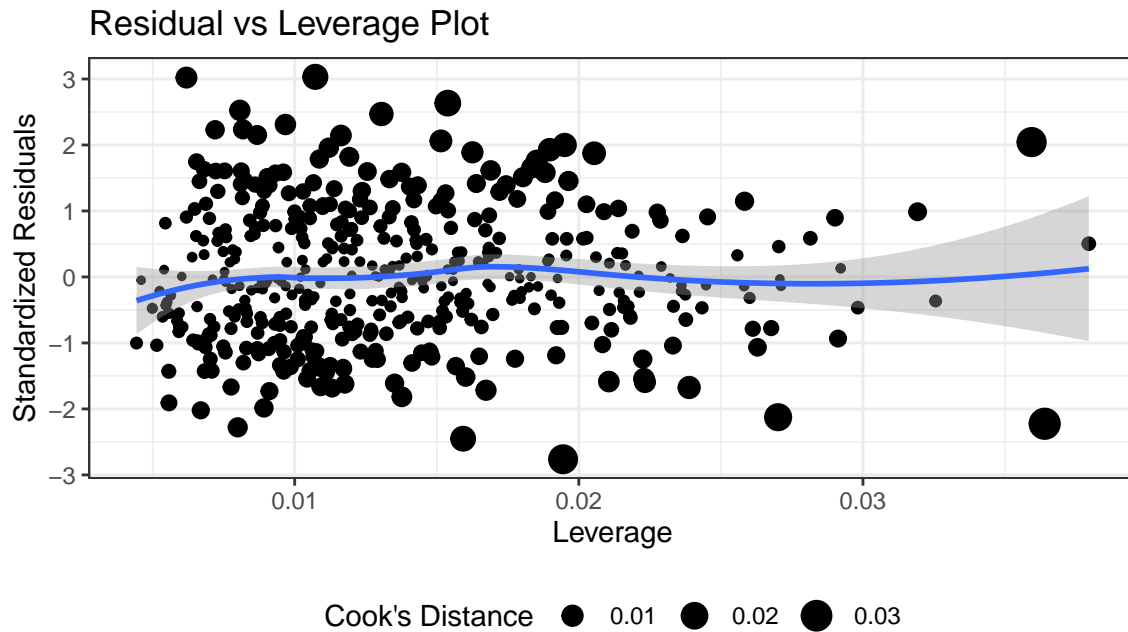
```
plot(x, y)
abline(mod, col = "red")
```

- Linear relationship and outliers (Residuals against fitted values)

```
plot(mod, which = 1)
```

- Homoscedasticity (Standardised residuals against fitted values)

```
plot(mod, which = 3)
```



- Normal-distribution of residuals (Q-Q plots of observed residuals against theoretical values under the Normal distribution)

```
plot(mod, which = 2)
```

- Influential variants: (Standardised residuals against Cook's distance)

```
plot(mod, which = 5)
```

Prediction using linear models

Assume we have a database with n type 2 diabetes cases, where we have measured the following data:

- y : quantitative measure of disease progression one year after baseline (vector)
- x : predictor matrix including clinical data (age, sex, bmi), blood pressure and triglycerides
- This is our training data y_{train} and x_{train} .

For a new case we only have the predictor matrix x_{new} , but not y_{new} .

Goal: For each new type 2 diabetes case we want to predict y_{new} , his/her progression one year later.

lm(): Predictions

- Use the linear model to learn a prediction rule from the training data, where both x and y are observed on the same individuals.

```
lm_train <-  
  lm(formula = y_train ~ age + sex + bmi + map + ltg, data = x_train)
```

- Predict the outcome based on the prediction rule and the predictors of the new data.

```
predict.lm(lm_train, x_new)
```

Take away: Linear models

- Motivation why to use linear models (To understand and to predict)
- Model fit using ordinary least squares
- Interpretation of the regression coefficients
- Residuals and fitted values
- Model diagnostics
- Using the linear model to predict